cipher
Pharmaceuticals Limited

VIA CERTIFIED MAIL, RETURN RECEIPT REQUESTED

General Counsel
Abbott Laboratories Inc.
Pharmaceutical Products Division
100 Abbott Park Road
Abbott Park, Illinois 60064-6400

General Counsel
Laboratories Fournier S.A.
9 rue Petitot
2100 Dijon, France

Re: Cipher NDA No. 21-612 for Fenofibrate Capsules 50, 100, 150 and 160 mg; Notice of Certification of Invalidity and Noninfringement of U.S. Patent No. 6,652,881 B2; and Offer of Confidential Access to Application

Dear Counsel:

As required by Section 505(b)(3) of the Federal Food, Drug and Cosmetic Act ("Act") (21 U.S.C. § 355(b)(3)), as amended by Title XI of the Medicare Prescription Drug, Improvement and Modernization Act, Pub. L. No. 108-173, 117 Stat. 2066 (2003), notice is hereby given to Abbott Laboratories Inc. ("Abbott"), as the holder of approved New Drug Application ("NDA") No. 21-203 for TRICOR® (fenofibrate) 54 mg and 160 mg tablets and the exclusive licensee of U.S. Patent No. 6,652,881 B2 ("the '881 patent"), and to Laboratories Fournier S.A. ("Fournier"), as the record owner of the '881 patent, that the Food and Drug Administration ("FDA") has received NDA No. 21-612, submitted by Cipher Pharmaceuticals Ltd. ("Cipher"), for Fenofibrate Capsules 50, 100, 150 and 160 mg.

Suite 201, Lauriston, Collymore Rock
St. Michael, Barbados
Tel: (246) 228-9663; Fax: (246) 228-8329

In accordance with 21 C.F.R. § 314.52, the following information is hereby provided:

- The NDA contains the required bioavailability or bioequivalence data.
- The NDA number for the application is 21-612.
- The established name for the proposed drug product is CIP-FENOFIBRATE.
- The active ingredient, strength, and dosage form of the product are as follows:
  fenofibrate, 50, 100, 150 and 160 mg capsule dosage forms.

With its NDA, Cipher has submitted a "paragraph IV certification," pursuant to Section 505(b)(2)(A)(iv) of the Act (21 U.S.C. § 355(b)(2)(A)(iv)), that its proposed fenofibrate capsules, 50, 100, 150 and 160 mg, will not infringe the '881 patent and/or that the '881 patent is invalid.

The '881 patent, expiring on or about January 9, 2018, contains no valid claims that would be infringed by the manufacture, use, or sale of Cipher's proposed fenofibrate 50, 100, 150 and 160 mg capsules.

In accordance with 21 U.S.C. § 355(b)(3)(D)(ii), as amended by Title XI of the Medicare Prescription Drug, Improvement and Modernization Act, Pub. L. No. 108-173, 117 Stat. 2066 (2003), and 21 C.F.R. §§ 314.52(c)(6)(i), (ii), the factual and legal bases for this paragraph IV certification and the statement that the '881 patent will not be infringed and/or that such patent is invalid is set forth below in Sections I-III of this notice letter.

Furthermore, in accordance with 21 U.S.C. § 355(c)(3)(D)(i)(III), as amended by Title XI of the Medicare Prescription Drug, Improvement and Modernization Act, Pub. L. No. 108-173, 117 Stat. 2066 (2003), this notice letter also includes, and Cipher hereby extends, an "Offer of Confidential Access to Application" to Abbott and Fournier under the specific restrictions set forth below in Section IV of this notice letter.

Suite 201, Lauriston, Collymore Rock
St. Michael, Barbados
Tel: (246) 228-9663; Fax (246) 228-8329

I. Cipher's Fenofibrate Product And Process.

The Cipher's NDA product is a gelatin capsule containing fenofibrate. This product is prepared by the Cipher process, namely melting and blending at 80 degrees centigrade polyglyceride (Gelucire 44/14) and PEG 8,000 and 20,000, then adding fenofibrate to the hot mixture and mixing until the fenofibrate is dissolved. The Cipher process also involves adding hydroxypropylcellulose and sodium starch glycolate and maintaining the mixture at 75 degrees centigrade. This molten mixture is then filled in a liquid state into hard gelatin capsules, and when cooled sets as a "paste" in the capsule.

Further details of Cipher's NDA product and process are set forth in U.S. Patent No. 5,545,628 to Deboeck *et al.*, as well as Cipher's confidential NDA documents and fenofibrate product samples that have already been provided to Abbott and Fournier pursuant to a Confidentiality Agreement between the parties. Pursuant to the restrictions in that Confidentiality Agreement, Cipher hereby authorizes Abbott and Fournier to access those NDA documents and fenofibrate product samples for purposes of determining whether a good faith infringement action can be brought. In Section IV of this notice letter, Cipher also extends, pursuant to the restrictions set forth herein, an "Offer of Confidential Access to Application" as required by § 355(c)(3)(D)(i)(III).

II. Legal Standards.

A. Patent Infringement.

Any patent infringement analysis consists of a two-step process: determining the scope of the claims, a legal issue for the Court, and comparing the accused device to the claims, a factual question. *Carroll Touch, Inc. v. Electro Mech. Sys., Inc.*, 15 F.3d 1573, 1576 (Fed. Cir. 1993); *see also Cybor Corp. v. FAS Techs., Inc.*, 138 F.3d 1448, 1456 (Fed. Cir. 1998) (en banc) (claim construction is an issue of law, subject to *de novo* review). A claim may be infringed either: (1) literally; or, (2) under the judicially created doctrine of equivalents.

Literal infringement requires a patentee to prove that every limitation of the asserted claim is literally met by the accused device. *Enercon v. Int'l Trade Comm'n*, 151 F.3d 1376, 1384 (Fed. Cir. 1998); *Amhil Enters. Ltd. v. Wawa, Inc.*, 81 F.3d 1554, 1562 (Fed. Cir. 1996) (literal infringement occurs when "the

Suite 201, Lauriston, Collymore Rock
St. Michael, Barbados
Tel: (246) 228-9663; Fax (246) 228-8329

properly construed claim reads on the accused device exactly"). The failure to meet even a single element within a claim mandates a finding that the accused product does not infringe the patent. *Laitram Corp. v. Rexnord, Inc.*, 939 F.2d 1533, 1535 (Fed. Cir. 1991).

The Supreme Court in *Warner-Jenkinson* held that even in instances where the claims do not read literally on the accused product or method, the patentee may look to the doctrine of equivalents to prove infringement. *Warner-Jenkinson Co. v. Hilton Davis Chem. Co.*, 520 U.S. 17, 21 (1997); *see also Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co., Ltd.*, 535 U.S. 722 (2002). Infringement under the doctrine of equivalents requires the patentee to show, for each claim asserted, the presence of each and every claim element or its substantial equivalent in the accused device. *Warner-Jenkinson*, 520 U.S. at 40 (applying the doctrine of equivalents analysis to the individual claim limitations, not the invention as a whole); *Wolverine World Wide, Inc. v. Nike, Inc.*, 38 F.3d 1192, 1199 (Fed. Cir. 1994).

III. Cipher Does Not And Will Not Infringe Any Of The Claims Of The '881 Patent.

Cipher's proposed fenofibrate product does not and will not infringe any of the claims of the '881 patent. The '881 patent has 41 total claims, 8 of which are independent claims, and recite as follows:

> 1. A composition comprising micronized fenofibrate, wherein the composition has a dissolution of at least 10% in 5 minutes, 20% in 10 minutes, 50% in 20 minutes and 75% in 30 minutes, as measured using the rotating blade method at 75 rpm according to the European Pharmacopoeia, in a dissolution medium constituted by water with 2% by weight polysorbate 80 or 0.025 M sodium lauryl sulfate.
>
> 6. An orally administrable tablet comprising micronized fenofibrate, wherein the tablet has a dissolution of at least 10% in 5 minutes, 20% in 10 minutes, 50% in 20 minutes and 75% in 30 minutes, as measured using the rotating blade method at 75 rpm according to the European Pharmacopoeia, in a

Suite 201, Lauriston, Collymore Rock
St. Michael, Barbados
Tel: (246) 228-9663; Fax (246) 228-8329

dissolution medium constituted by water with 2% by weight polysorbate 80 or a dissolution medium constituted by water with 0.025 M sodium lauryl sulfate.

11. A composition comprising micronized fenofibrate and at least one polymer, wherein the composition has a dissolution of at least 10% in 5 minutes, 20% in 10 minutes, 50% in 20 minutes and 75% in 30 minutes, as measured using the rotating blade method at 75 rpm according to the European Pharmacopoeia, in a dissolution medium constituted by water with 2% by weight polysorbate 80 or 0.025 M sodium lauryl sulfate.

15. A composition comprising at least one inert carrier and one or more outer layers comprising micronized fenofibrate, wherein the composition has a dissolution of at least 10% in 5 minutes, 20% in 10 minutes, 50% in 20 minutes and 75% in 30 minutes, as measured using the rotating blade method at 75 rpm according to the European Pharmacopoeia, in a dissolution medium constituted by water with 2% by weight polysorbate 80 or 0.025 M sodium lauryl sulfate.

22. A composition comprising granulates which comprise micronized fenofibrate; wherein the composition has a dissolution of at least 10% in 5 minutes, 20% in 10 minutes, 50% in 20 minutes and 75% in 30 minutes, as measured using the rotating blade method at 75 rpm according to the European Pharmacopoeia, in a dissolution medium constituted by water with 2% by weight polysorbate 80 or a dissolution medium constituted by water with 0.025 M sodium lauryl sulfate.

27. An orally administrable tablet comprising granulates, wherein the granulates comprise

Suite 201, Lauriston, Collymore Rock
St. Michael, Barbados
Tel: (246) 228-9683; Fax (246) 228-8329

micronized fenofibrate, and wherein the tablet has a dissolution of at least 10% in 5 minutes, 20% in 10 minutes, 50% in 20 minutes and 75% in 30 minutes, as measured using the rotating blade method at 75 rpm according to the European Pharmacopoeia, in a dissolution medium constituted by water with 2% by weight polysorbate 80 or a dissolution medium constituted by water with 0.025 M sodium lauryl sulfate.

32. An orally administrable capsule comprising granulates, wherein the granulates comprise micronized fenofibrate, and wherein the capsule has a dissolution of at least 10% in 5 minutes, 20% in 10 minutes, 50% in 20 minutes and 75% in 30 minutes, as measured using a rotating blade method at 75 rpm according to the European Pharmacopoeia, in a dissolution medium comprising water with 2% by weight polysorbate 80 or a dissolution medium comprising water with 0.025 M sodium lauryl sulfate.

37. A granulate comprising micronized fenofibrate, wherein the granulate has a dissolution of at least 10% in 5 minutes, 20% in 10 minutes, 50% in 20 minutes and 75% in 30 minutes, as measured using the rotating blade method at 75 rpm according to the European Pharmacopoeia, in a dissolution medium constituted by water with 2% by weight polysorbate 80 or a dissolution medium constituted by water with 0.025 M sodium lauryl sulfate.

Each independent claim of the '881 patent covers a composition comprising "micronized fenofibrate." The term "micronized" is defined in the specification as "a substance in a particulate form, the dimensions of the particle being less than or equal to about 20 um." ('881 patent, col. 4, lines 27-29). As explained in Cipher's summary judgment papers submitted in *Abbott Laboratories Inc. v. Cipher Pharmaceuticals Ltd.*, Civil Nos. 03-1421 and 03-2067 (DRD) (D.P.R.), the scope of this definition is further limited by the scope and content of the prior art, and admissions made to the U.S. Patent and Trademark

Suite 201, Lauriston, Collymore Rock
St. Michael, Barbados
Tel: (246) 228-9663; Fax (246) 228-8329

Office ("PTO"). The Cipher product does not contain micronized fenofibrate and does not contain particles in dimensions which are less than or equal to about 20 um.

Importantly, during prosecution, the Examiner cited U.S. Patent No. 5,545,628 by Deboeck that describes and is specifically directed to the Cipher product. The patentee carefully distinguished its claimed, micronized product from the composition of Deboeck: "the presently claimed invention comprises a micronized fenofibrate while Deboeck does not require any particular particle size (Deboeck at column 2, lines 40-42). In fact, Deboeck seeks to avoid micronization (Deboeck at column 2, lines 4-7). Accordingly, Deboeck teaches away from the presently claimed micronized fenofibrate." (Response of January 26, 2001, page 7). The language of Deboeck at column 2, lines 4-7, cited above by the patentee states that: "The present invention is also particularly advantageous for the production of oral solid dosage forms which can be prepared by melting the excipients in which the fenofibrate is soluble, where by particle size specifications are not required."

Moreover, in the '670 patent, which is the parent of the '881 patent, the patentee carefully distinguished "micronized" material from the "molten solution" of Deboeck (Response of November 17, 1999, page 5, emphasis in original). The prosecution history of the '670 patent is highly relevant to the claim interpretation of the '881 patent. The '670 patent is the parent of the '881 patent and contains the same specification as the '881 patent. Both patents contain claims covering micronized fenofibrate compositions. Moreover, the '670 and '881 patents were examined by the same primary examiner at the PTO. Based on the patentee's arguments over Deboeck in both the '881 patent prosecution and in the '670 patent prosecution, a reviewing court should not interpret "micronized" as including or being the equivalent of "molten."

Additional elements, such as the claim term "granulates," as well as the adoption of specified dissolution profiles, were similarly limited by the scope and content of the prior art, and during the prosecution history of the patent.

Under U.S. law, a court would first interpret the scope and meaning of patent claims and then compare the properly construed claims to the allegedly infringing product. The absence of even one claim element avoids literal infringement. Therefore, to establish literal infringement, every limitation set forth in a claim must be found in the accused product.

Suite 201, Lauriston, Collymore Rock
St. Michael, Barbados
Tel: (246) 228-9663; Fax (246) 228-8329

In the '881 patent, the claims must be interpreted as containing fenofibrate in a specific form, *i.e.*, in micronized form; meeting certain dissolution characteristics and, in various claims, the use of granulates; tablets; inert hydrosoluble carriers; and the like. The independent claims recite these limitations and the dependent claims incorporate such limitations by virtue of dependency. Because the Cipher product is a capsule, does not contain granulates and does not involve micronization of any of the fenofibrate alone or in combination with another ingredient, and the Cipher product does not in fact contain micronized ingredients, these and other elements are absent from the Cipher product and Cipher process, and therefore the product proposed by Cipher's NDA specifications avoids literal infringement

Even where no literal infringement exists, a product may nevertheless infringe a patent under the doctrine of equivalents, which permits a court to extend the effective scope of patent protection beyond a claim's literal wording. However, even under the doctrine of equivalents, each element or equivalent of such element in a claim must be present. It is clear from the above analysis that the Cipher product fails to contain many of the elements in the claims.

More importantly, however, is the fact that with regard to all of the claims in the '881 patent, is the effect of prosecution history estoppel. For example, the patentees, in the '881 patent, relied upon the micronization feature of their invention to obtain allowance of the claims. During the prosecution history for the '881 patent, the patentees repeatedly distinguished micronized fenofibrate from the fenofibrate subjected to melting processes used by Cipher. The same holds true for additional elements, such as those involving granulates and dissolution profiles. In view of such statements and arguments, it is doubtful that a reviewing court would expand the scope of the micronization feature of the claims to include "melting."

Therefore, the Cipher product and Cipher process avoid literal infringement and infringement under the doctrine of equivalents of all of the claims in the '881 patent.

* * *

Cipher affirmatively states that it may have further bases, in addition to those stated above, supporting its invalidity and/or noninfringement positions under 35 U.S.C. §§ 101 *et seq*, (including §§ 102(a), (c)-(g) and § 112). In

Suite 201, Lauriston, Collymore Rock
St. Michael, Barbados
Tel: (246) 228-9663; Fax (246) 228-8329

particular, to the extent infringement of the '881 patent by Cipher's proposed product is alleged, under the principles set forth in *Vanmoor v. Wal-Mart Stores, Inc.*, 201 F.3d 1363 (Fed. Cir. 2000), the '881 patent is invalid as anticipated under 35 U.S.C. § 102(b). Further, additional bases bearing on the validity, noninfringement, and/or enforceability of the patent described herein, and to which Cipher is required to certify, may develop in the event of litigation between the parties. Cipher expressly reserves the right to assert additional defenses and grounds bearing on the validity, noninfringement, and/or enforceability of the patent described herein in the event of litigation between the parties.

Receipt of this notice begins the 45-day period provided for in Section 505(c)(3)(C) of the Hatch-Waxman Amendments to the Federal Food, Drug and Cosmetic Act. The NDA will be amended with a copy of the return receipt for this notice, as required by 21 C.F.R. § 314.52(e).

The following person is authorized to accept service of process on behalf of Cipher:

Arthur M. Deboeck
Galephar P.R. Inc.
Road 198 No. 100 km 14.7
Juncos Industrial Park
Juncos, Puerto Rico 00777-3873
Tel: (787) 713-0340
Fax: (787) 713-0344
Email: adeboeck@galephar.com

A courtesy copy of any complaint should also be faxed to Cipher's litigation counsel, as follows:

William A. Rakoczy
LORD, BISSELL & BROOK LLP
115 South LaSalle Street
Chicago, IL 60603
Tel: (312) 443-0329
Fax: (312) 896-6329
wrakoczy@lordbissell.com

Suite 201, Lauriston, Collymore Rock
St. Michael, Barbados
Tel: (246) 228-9663; Fax (246) 228-8329

IV. Offer Of Confidential Access To Application

Pursuant to 21 U.S.C. § 355(c)(3)(D), as amended by Title XI of the Medicare Prescription Drug, Improvement and Modernization Act, Pub. L. No. 108-173, 117 Stat. 2066 (2003), this notice letter includes an Offer of Confidential Access to Application. As required by § 355(c)(3)(D)(i)(III), and pursuant to certain restrictions described below, Cipher offers to provide Abbott and Fournier with confidential access to certain information from its NDA No. 21-612 for the sole and exclusive purpose of determining whether an infringement action referred to in § 355(c)(3)(C) can be brought.

Section 355(c)(3)(D)(i)(III) allows Cipher to impose restrictions "as to persons entitled to access, and on the use and disposition of any information accessed, as would apply had a protective order been entered for the purpose of protecting trade secrets and other confidential business information." That provision also grants Cipher the right to redact its NDA in response to a request for Confidential Access under this offer.

As permitted by statute, Cipher imposes the following terms and restrictions on its Offer of Confidential Access:

(1) Cipher will permit confidential access to certain information from its proprietary NDA No. 21-612 to attorneys from one (1) outside law firm representing Abbott and Fournier; provided, however, that such attorneys do not engage, formally or informally, in patent prosecution for Abbott or Fournier. Such information (hereinafter, "Confidential Cipher Information") shall be marked with the legend "CONFIDENTIAL".

(2) The attorneys from the outside law firm representing Abbott and Fournier shall not disclose any Confidential Cipher Information to any other person or entity, including Abbott and Fournier employees, outside scientific consultants, and/or other outside counsel retained by Abbott and Fournier, without the prior written consent of Cipher's outside litigation counsel, LORD, BISSELL & BROOK LLP.

(3) As provided by § 355(c)(3)(D)(i)(III), Abbott and Fournier's outside law firm shall make use of the Confidential Cipher Information for

Suite 201, Lauriston, Collymore Rock
St. Michael, Barbados
Tel: (246) 228-9663; Fax (246) 228-8329

the sole and exclusive purpose of determining whether an action referred to in § 355(c)(3)(C) can be brought and for no other purpose. By way of example only, the Confidential Cipher Information shall not be used to prepare or prosecute any future or pending patent application by Abbott and Fournier, or in connection with any filing to, or communication with, the FDA relating to Cipher's NDA No. 21-612. Abbott and Fournier's outside law firm agrees to take all measures necessary to prevent unauthorized disclosure or use of the Confidential Cipher Information, and that all Confidential Cipher Information shall be kept confidential and not disclosed in any manner inconsistent with this Offer of Confidential Access. Abbott and Fournier's outside law firm further agrees never to use Confidential Cipher Information, directly or indirectly, in competition with Cipher, nor will it allow any other person or entity to do so.

(4) The Confidential Cipher Information disclosed is, and remains, the property of Cipher. By providing the Confidential Cipher Information, Cipher does not grant Abbott and Fournier and/or Abbott and Fournier's law firm any interest in or license for the Confidential Cipher Information.

(5) Abbott and Fournier's law firm shall, within thirty-five (35) days from the date that it first receives the Confidential Cipher Information, return to Cipher's outside litigation counsel, LORD, BISSELL & BROOK LLP, all Confidential Cipher Information and any copies thereof. Abbott and Fournier's law firm shall return to LORD, BISSELL & BROOK LLP all Confidential Cipher Information before any infringement suit is filed by Abbott and Fournier, if suit is commenced before this 35-day period expires. In the event that Abbott and Fournier opts to file suit, none of the information contained in or obtained from any Confidential Cipher Information that Cipher provides will be included in any publicly-available complaint or other pleading.

(6) Nothing in this Offer of Confidential Access shall be construed as an admission by Cipher regarding the validity, enforceability, and/or infringement of any U.S. Patent. Further, nothing herein shall be construed as an agreement or admission by Cipher with respect to

Suite 201, Lauriston, Collymore Rock
St. Michael, Barbados
Tel: (246) 228-9663; Fax (246) 228-8329

the competency, relevance, or materiality of any such Confidential Cipher Information, document, or thing. The fact that Cipher provides Confidential Cipher Information upon request of Abbott and Fournier shall not be construed as an admission by Cipher that such Confidential Cipher Information is relevant to the disposition of any issue relating to any alleged infringement of the Abbott and Fournier's patents, or to the validity or enforceability of any such patents.

(7) The attorneys from Abbott and Fournier's outside law firm will acknowledge in writing their receipt of a copy of these terms and restrictions prior to production of any Confidential Cipher Information. Such written acknowledgement shall be provided to Cipher's outside litigation counsel, LORD, BISSELL & BROOK LLP.

(8) This Offer of Confidential Access shall be governed by the laws of the State of Illinois.

Section 355(c)(3)(D)(i)(III) of the Act provides that any request for access that Abbott and Fournier make under this Offer of Confidential Access "shall be considered acceptance of the offer of confidential access with the restrictions as to persons entitled to access, and on the use and disposition of any information accessed, contained in [this] offer of confidential access" and that the "restrictions and other terms of [this] offer of confidential access shall be considered terms of an enforceable contract." Thus, to the extent that Abbott and Fournier request access to Confidential Cipher Information, they necessarily accept the terms and restrictions outlined above. Written notice requesting access under this Offer of Confidential Access should be made to:

Suite 201, Lauriston, Collymore Rock
St. Michael, Barbados
Tel: (246) 228-9663; Fax (246) 228-8329

William A. Rakoczy
LORD, BISSELL & BROOK LLP
115 South LaSalle Street
Chicago, IL 60603
Tel: (312) 443-0329
Fax: (312) 896-6329
wrakoczy@lordbissell.com

By providing this Offer of Confidential Access to Application, Cipher maintains the right and ability to bring a Declaratory Judgment action under 28 U.S.C. §§ 2201 *et seq.*, pursuant to 21 U.S.C. § 355(c)(3)(D).

Regards,

Ian W. French
Chief Scientific Officer
Cipher Pharmaceuticals Ltd.

Feb. 3, 2004
Date

Suite 201, Lauriston, Collymore Rock
St. Michael, Barbados
Tel: (246) 228-9663; Fax (246) 228-8329